REMARKS

Status of the Claims

Claim 10 is now cancelled; claims 6-7 were previously cancelled.

Claims 1-5 and 8-9 are currently pending and under consideration.

Examiner Interview

Applicants would like to thank the Examiner for her time today, February 24, 2009, to discuss the topics at issue in this after-final response.

Double Patenting

The Examiner has provisionally rejected claims 1, 2, 4, 6, 8 and 9 on the grounds of nonstatutory obviousness-type double patenting over copending Application Nos. 10/534,915 and 10/532,319.

If a "provisional" double patenting rejection in one application is the only rejection remaining in that application, the examiner should then withdraw the rejections and permit the application to issue as a patent. Application Nos. 10/534,915 and 10/532,319 are not currently allowed. Accordingly, Applicants submit if these provisional rejections are the only outstanding rejections, the present claims should be allowed. However, Applicants will consider filing Terminal Disclaimers when the present claims are indicated as otherwise allowable if/when Application Nos. 10/534,915 and 10/532,319 are allowed.

At the 2/24/09 interview, Applicants and the Examiner have agreed that the Applicants will promptly notify the Examiner of any change in status in the co-pending applications.

Claim Rejections – 35 U.S.C. §102

The Examiner has rejected claim 10 under 35 U.S.C 102(b) as being anticipated by Jannes et al. (Final Action page 3)

Without acquiescing to the rejection and solely to facilitate prosecution, Applicants have cancelled claim 10. Applicants respectfully request withdrawal of the §102(b) rejection. At the 2/24/09 interview, the Examiner has agreed to withdraw this rejection.

Claim Rejections – 35 U.S.C. §103

The Examiner has rejected claims 1-6 and 8-9 under 35 U.S.C 103(a) as being unpatentable over Jannes et al. in view of de Silva et al. (Final Action page 6) The Examiner asserts, in part, that it would have been *prima facie* obvious to one of ordinary skill in the art to have extended the method taught by Jannes to incorporate the methods of determining and monitoring the temperature dependence of hybridization as taught by de Silva. Further, the Examiner asserts that all of the claimed elements were known and disclosed by Jannes and de Silva. (Final Action pages 9-10)

Applicants respectfully traverse the rejection.

- One reaction vessel

The Examiner states that Jannes Example 3 discloses the amplification and detection occurring on the membrane test strip, which meets the limitation of one reaction vessel. (Final Action page 5). As discussed at the 2/24/09 interview, Applicants assert that Jannes Example 3 discloses amplification and detection taking place in separate reaction vessels. One of ordinary skill in the art would readily recognize in Jannes Example 3 and throughout the Jannes specification and other examples that the steps of the amplification of the spacer region by polymerase chain reaction and the hybridization with immobilized probes on a membrane strip are done sequentially; 1st the amplification is performed, 2nd the resulting PCR fragments are hybridized to immobilized probes. This sequential process is described in a straight-forward manner in Jannes on page 13, last paragraph: "After amplification ... the amplified product is contacted with the probes on the membrane and the hybridization is carried out for 1 or 1,5 h."

Claim 1 of the instant invention requires: "b) subjecting said clinical sample to at least one amplification step and at least one detection step in one reaction vessel...". Jannes does not teach or suggest this limitation of the amplification step and the detection step being performed concurrently in one reaction vessel.

- Internal control template

The Examiner states that Jannes et al teach assays applying oligonucleotide probes, including negative or positive control oligonucleotides, and disclose the use of primers with a known sequence with a primer binding site complementary to at least one set of specific amplification primers; therefore Jannes anticipates the internal control template as required by the instant invention. (Final Action page 5, also page 10) As discussed at the 2/24/09 interview, Applicants assert that Jannes teaches a type of external control – control oligonucleotides that are used in the hybridization step. Jannes page 13, refers to Saiki et, 1989, for reference to the Line Probe Assay and use of control oligonucleotides. Jannes (and/or Saiki) does not teach the use of an internal control template as defined by the instant invention.

Further, as discussed at the 2/24/09 interview, Applicants assert that de Silva does not teach the use of an internal control template. The beta-globin amplification taught by de Silva is an external control. The amplification is performed by an additional set of amplification reagents in a separate reaction vessel than the amplification of the primary target of interest (Factor V Leiden) and therefore cannot be considered an internal control as defined by the instant invention.

The Examiner notes that page 18 lines 23-31 of the application as filed does not state that internal controls cannot be in a separate reaction vessel. (Final Action page 11) However, it is well understood by one skilled in the art, and provided in the specification as filed, that an internal control template is in the same reaction vessel with the amplification of interest. See the specification on page 18 lines 23-25:

> "In order to avoid false negative results due to inhibitory residual components which may be present in the clinical specimen and for quantification purposes, it has been proven to be particular advantageous, if an internal control template is added."

It is clear from the citation above as well as from the Examples provided in the specification as filed that the internal control template is added to the reaction of interest, not run in addition to the reaction of interest. See Example I beginning on page 24 line 15, in particular the Method section B beginning on page 26 line 18 of the application as filed, where the internal control template "IC" was either added to the mastermix, or added to the specimen which is then processed and added to mastermix.

External controls such as the control oligonucleotides of Jannes and the beta-globin amplification described by de Silva do not provide the same level of information as an internal control as required by the instant invention. These external controls do not provide information relating to potential false-negative results of the amplification of interest due to inhibitory residual components which may be present in the clinical specimen, nor do these external controls provide direct quantification information related to the amplification of interest.

All of the claimed elements of the instant invention, specifically the use of one reaction vessel and an internal control template, were NOT disclosed by Jannes and de Silva. The cited references, or combination of the references, do not teach or suggest all of the claim limitations as required by the instant invention. Because the Examiner has not established a *prima facie* case of obviousness, for the reasons provided above and as discussed at the 2/24/09 interview, Applicants respectfully request the reconsideration and withdrawal of the §103 rejections.

Claim Rejections – 35 U.S.C. §112

The Examiner has rejected claims 1-5 and 8-10 under 35 U.S.C 112, first paragraph, as failing to comply with the written description requirement. (Final Action page 14) The Examiner asserts that Applicants did not point to support in the specification for "one reaction vessel".

Applicants wish to direct the Examiner again to the entirety of page 19 of the specification for discussion of homogeneous reaction embodiments. The term "homogeneous" is well understood to one skilled in the art to mean that the reaction is being performed in one vessel, as clearly described on page 19 beginning at line 12:

"In the homogenous embodiment ... reagents for both the amplification and the detection step are added to the specimen prior to the beginning of amplification step ba)."

Further definition can be found on page 19, lines 29-34:

"According to the present invention, the amplification step ba) and the detection step bb) are preferably carried out subsequently in a homogenous assay format, characterized in that the one or more hybridization reagents are already present within the reaction mixture during the amplification step. In other words, amplification step ba) and detection step bb) are carried out within the same reaction vessel and without addition of further reagent between the steps." (emphasis added)

Applicant assert that "one reaction vessel" is well supported in the specification as originally filed and respectfully request withdrawal of the 112 rejections. At the 2/24/09 interview, the Examiner has agreed to withdraw this rejection.

CONCLUSION

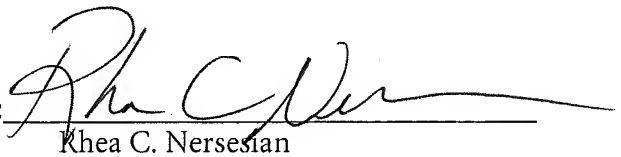
Applicants again thank the Examiner for the opportunity to discuss this application in the interview today, February 24, 2009. Applicants respectfully assert that the present application is in condition for allowance and request that the Office issue a timely Notice of Allowance. If the Examiner believes that a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-730-8566.

Applicants assert that no fee is due with the filing of this After-Final Response. However, the commissioner is hereby authorized to grant any extensions of time that may be required to enter this Response and charge any fees or credit any overpayments to Deposit Account No. 50-0812.

Please direct all future correspondences to: Customer No. 22829.

Respectfully submitted,

Date: February 24, 2009

By: 
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